Abnormal bacterial colonisation of the genital tract and subsequent preterm delivery and late miscarriage

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Abstract

***Objective*—To find out whether women with bacterial vaginosis detected early in pregnancy are at increased risk of preterm delivery.**

***Design*—Prospective description cohort study.**

***Setting*—Antenatal clinic in a district general hospital.**

***Subjects*—783 women examined during their first antenatal clinic visit and screened for recognised risk factors for preterm delivery and the presence of bacterial vaginosis or intermediate abnormal flora detected by examination of a vaginal smear stained by Gram's method.**

***Main outcome measures*—Gestational age at delivery classified as late miscarriage (16-24 weeks' gestation), preterm delivery (24-37 weeks' gestation), term delivery ($\geq$ 37 weeks' gestation).**

***Results*—Multiple logistic analysis showed that there was an increased incidence of preterm delivery in women with a previous preterm delivery (9/24; odds ratio 25; 95% confidence interval 9 to 70; $P < 0{\cdot}001$) and bacterial vaginosis (9/115; 2·8; 1·1 to 7·4; $P = 0{\cdot}04$). A further logistic analysis of data from women recruited before 16 weeks' gestation showed that preterm deliveries or late miscarriages occurred more often in women with bacterial vaginosis (12/77; 5·5; 2·3 to 13·3; $P < 0{\cdot}001$).**

***Conclusions*—Late miscarriage and preterm delivery are associated with the presence of bacterial vaginosis in early pregnancy. This is independent of recognised risk factors such as previous preterm delivery.**

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Introduction

Preterm delivery is the most important cause of perinatal mortality and morbidity. There are many causes and it remains incompletely understood. The most powerful predictor of preterm delivery is a history of such a delivery, but this is of no use in the case of primigravidas. Scoring systems designed to identify those women at increased risk of preterm delivery by incorporating recognised risk factors have lacked sufficient specificity to be clinically useful.[1] Even if a group of women at risk of preterm delivery could be identified accurately there is no proof that prophylactic measures would be helpful since bed rest, cervical cerclage, and long term obstetric treatment have failed to provide any benefit.[2]

There is increasing evidence that ascending infection from the lower genital tract is an important cause of preterm labour.[3-6] Sexually transmitted infections such as syphilis, gonorrhoea, trichomoniasis, and chlamydial infections have been implicated in some, but not all, studies. More attention is being given to bacterial vaginosis, a condition in which there is an overgrowth of anaerobic and other bacteria in the vagina with a corresponding decrease in the number of lactobacilli. In both case-control and prospective studies bacterial vaginosis has been associated with preterm deliveries. Such information may be of little value when a woman presents in preterm labour since by this time there may already be substantive and irreversible changes in the cervix uteri which render attempts to reverse the process unacceptable or likely to fail. The detection of abnormal bacterial colonisation of the genital tract as a predictor of preterm labour may be of use,[7] but to be of value a screening test should be simple, inexpensive, and capable of indicating the outcome of pregnancy early in gestation. To this end we have used Gram's method of staining to detect abnormal vaginal bacterial colonisation indicative of bacterial vaginosis and have examined the prevalence of bacterial vaginosis in early pregnancy and assessed its association with adverse outcomes of pregnancy.

Subjects and methods

Women between nine and 24 weeks of gestation who were making their first antenatal visit to Northwick Park Hospital, Harrow, were recruited to a prospective observational study. This had been approved by the local ethics committee. The hospital is a district general hospital which serves a predominantly middle class population with a low incidence of sexually transmitted diseases. A total of 783 women were recruited but subsequently 65 were excluded from the analysis. Seven were found not to be pregnant; nine had elective deliveries before 37 weeks of gestation; 11 took antibiotics after bacterial vaginosis was diagnosed; three were carrying fetuses with lethal congenital malformations; 11 were carrying twins; four underwent termination of pregnancy; and 20 were lost to follow up. In calculating the size of the population to be studied we assumed an incidence of bacterial vaginosis of 5% and an incidence of premature birth of 7% and that women with bacterial vaginosis would be 3·8 times as likely to have preterm delivery as women with normal flora.[8] A sample size of 1000 gives a power of 91%.

Recruitment was stopped after 783 women had been enrolled as the incidence of bacterial vaginosis was about double that assumed in the calculations of sample size.

Informed verbal consent to undergo examination was sought and then subjects completed a short questionnaire about current symptoms and previous urogenital infections. Cotton wool swabs were used through a non-lubricated vaginal speculum to sample the endocervix and posterior vaginal fornix. Both swabs were rolled on glass slides and the smears fixed immediately in methyl alcohol and allowed to dry in air. Then they were stained by Gram's method and read by one investigator (PEH) within two weeks of

collection, before information on the outcome of pregnancy was available. The slides were reviewed independently by a second investigator (CI), who was not informed of the nature of each case. If the two investigators came to different conclusions the slides were reviewed by both concurrently until agreement was reached. The results were not relayed to the clinician. If Gram negative diplococci had been detected in any cervical smears the clinician would have been informed.

The criteria for diagnosing bacterial vaginosis on the basis of Gram's stain, as described by Spiegel *et al*,[9] were used with the addition of an intermediate category. Thus, the flora were graded as grade I: normal (predominantly lactobacillus morphotypes); grade II: intermediate (reduced lactobacillus mixed with other morphotypes); grade III: abnormal (few or no lactobacillus morphotypes with greatly increased numbers of *Gardnerella vaginalis* or other morphotypes, or both). In addition, the presence of yeasts, sperm, and blood was recorded. After pregnancy the hospital notes were reviewed and the data relating to previous pregnancies, recognised risk factors for preterm labour, antenatal events, and delivery were recorded.

TABLE I—*Demographic data in relation to grade of flora in vagina of pregnant women*

Demographic variable	Grade of flora I	II	III	P value*
Mean (SD) age (years)	29 (4·8)	30 (5·2)	27 (5·0)	0·012
Mean (SD) height (cm)	161 (7·0)	161 (6·7)	162 (6·7)	0·304
Mean (SD) weight (kg)	62 (11·5)	61 (10·9)	64 (12·7)	0·421
No (%) of women with parity:				
0	257 (83)	12 (4)	42 (13)	
1	215 (82)	15 (6)	31 (12)	0·820
2	85 (86)	4 (4)	10 (10)	
⩾3	32 (82)	3 (8)	4 (10)	
Obstetric history:				
No previous pregnancy	190 (83)	8 (3)	31 (14)	
Previous abortion:				
No	224 (82)	18 (7)	31 (11)	0·443
Yes	175 (84)	8 (4)	25 (12)	
Previous preterm delivery:				
No	380 (83)	25 (6)	52 (11)	0·697
Yes	19 (79)	1 (4)	4 (17)	
Smoker:				
No	457 (85)	30 (6)	50 (9)	
Yes	86 (74)	2 (2)	28 (24)	< 0·001
Former	31 (79)	1 (3)	7 (18)	
Ethnic origin:				
White	361 (84)	16 (4)	55 (12)	
Afro-Caribbean	24 (57)	1 (2)	17 (41)	< 0·001
Asian	179 (86)	16 (8)	13 (6)	
Other	22 (92)	1 (4)	1 (4)	

*This P value tests hypothesis that all three grades of flora are same by using either χ^2 tests or analysis of variance.

TABLE II—*Outcome of pregnancy in women recruited before 24 weeks' gestation who delivered from 24 weeks' gestation*

Variable	No (%) who had preterm delivery	Total	Odds ratio (95% confidence interval)	P value
Grade of flora:				
I	17 (2·9)	584	1	0·04
II	1 (3·1)	32	2·8 (1·1 to 7·4)	
III	8 (9·6)	83		
Obstetric history:				
No previous pregnancy	9 (3·9)	231	1	
Previous preterm labour:				
No	9 (2·0)	450	1	< 0·001
Yes	9 (37·5)	24	24·8 (8·8 to 69·9)	
Ethnic origin:				
White	11 (2·6)	427	1	0·192
Afro-Caribbean	3 (7·3)	41	3·1 (0·8 to 12·9)	
Asian	9 (4·4)	206	2·0 (0·8 to 5·2)	
Other	2 (8·3)	24	4·3 (0·8 to 24·0)	

TABLE III—*Outcome of pregnancy in women recruited before 16 weeks' gestation who delivered from 16 weeks' gestation*

Variable	No (%) who had late miscarriage	No (%) who had preterm delivery	Total	Odds ratio (95% confidence interval)	P value
Grade of flora:					
I	4 (1·0)	9 (2·3)	384	1	< 0·001
II	1 (5·0)	0	20	5·5 (2·3 to 13·3)	
III	4 (7·0)	7 (12·3)	57		
Obstetric history:					
No previous pregnancy	0	6 (3·9)	154	1	
Previous preterm delivery:					
No	9 (3·0)	5 (1·7)	295	1	< 0·001
Yes	0	6 (33·3)	18	13·1 (4·0 to 42·6)	

STATISTICAL METHODS

Known confounding variables of age, smoking, ethnic origin, height, weight, previous abortions, and previous preterm delivery were identified before the statistical anlysis was performed. We used χ^2 tests or analyses of variance to compare the three grades of flora.

Women who had late miscarriages were excluded from the following analysis. The association between preterm delivery and each of these seven confounding variables was examined by using individual logistic regressions. All seven variables were included in a multiple logistic regression model and the effect of adding bacterial vaginosis into the model was assessed. This approach was used because confounding variables may go undetected when analysed individually but may collectively lead to considerable confounding.[10] The resulting model, however, had numerically unstable estimates of the parameters. We therefore selected a subset of the confounding variables for inclusion into a multiple logistic model and entered those variables which were significant ($P < 0·25$) in the individual logistic analyses into the multiple logistic model.[11]

The significance level of 0·25 was chosen as the inclusion criterion to ensure that all important confounding variables were entered into the model. The odds ratio for preterm deliveries and 95% confidence intervals are presented.

A similar analysis was performed for women who were recruited before 16 weeks' gestation. This analysis aimed to establish the association between preterm delivery or late miscarriage and bacterial vaginosis.

Results

Of the 718 women in the study who were evaluable, 589 had vaginal flora of grade I, 35 of grade II, and 87 of grade III; grade was not recorded for seven. Table I shows the demographic data according to the grade of flora. There were 22 missing values for smoking habit but only a small number of missing values for other variables, and these did not materially alter the comparisons. Most of the variables, including previous abortion and previous preterm delivery, were independent of grade of flora. Women who were currently smokers, however, significantly more often had grade III flora, as did Afro-Caribbean women. Of the 718 women, 679 had term deliveries, 27 preterm deliveries, and 12 late miscarriages.

An initial examination of the data showed an association between abnormal flora and preterm delivery and also late miscarriage. The association with late miscarriage had not been anticipated so two analyses of the data were performed. Table II shows the results for the 706 women screened before 24 weeks' gestation who delivered from 24 weeks' gestation. In the independent logistic analysis four variables had P values of $< 0·25$. These were grade of flora, previous preterm delivery, ethnic origin, and previous stillbirth. The first three of these were included into a multiple logistic regression analysis. Previous stillbirths were excluded because they occurred in only three women. Table III shows the results for the logistic analysis of the 467 women recruited before 16 weeks' gestation including those who had a late miscarriage. No woman miscarried before 16 weeks' gestation. In this analysis ethnic origin was not significant ($P > 0·25$) in the independent logistic analysis.

Thus in the first analysis (table II) preterm delivery was seen to occur in association with grade II and grade

III flora (odds ratio 2·8; 95% confidence interval 1·1 to 7·4). Women with at least one previous preterm delivery had a much greater chance of delivering preterm (24·8; 8·8 to 69·9). There was a non-significant trend for women of Afro-Caribbean or Asian origin to have a preterm delivery. In the second analysis (table III) late miscarriage and preterm delivery were associated with grade II and III flora (5·5; 2·3 to 13·3) and with a previous preterm delivery (13·1; 4·0 to 42·6).

Discussion

We found a significant association between abnormal bacterial colonisation of the genital tract detected early in pregnancy and preterm delivery and also late miscarriage. To our knowledge, the association with late miscarriage has not been recorded by others. Although there has been increasing evidence to implicate bacterial infection of the genital tract with a poor outcome of pregnancy, the number of micro-organisms that need to be considered has created a problem in understanding the role of each. In this regard an important virtue of the population we studied is the low prevalence of sexually transmitted diseases caused by *Neisseria gonorrhoeae*, *Chlamydia trachomatis*, and *Trichomonas vaginalis*. This is supported by only one woman having *T vaginalis* detected cytologically. Furthermore, in a previous study of women attending the antenatal clinic at this hospital, *C trachomatis* was found in only one of 179 women tested by means of a direct fluorescent antibody test (MicroTrak, Syva), and there were no cases of gonococcal infection (B J Thomas, personal communication). Thus, we have been able to examine the role of bacterial vaginosis without these confounding variables.

Bacterial vaginosis is diagnosed conventionally when at least three of four composite criteria are fufilled. This is laborious, and in this study we used Gram's method of staining which we and others have shown to be a simple, inexpensive, sensitive, specific, and reproducible way to diagnose bacterial vaginosis.[12 13] We categorised the vaginal flora as normal, intermediate, or abnormal. In the United States Hillier *et al* found an intermediate category, which was thought to represent a transitional pattern.[14] While our independent classification may not match theirs precisely, we are probably observing the same phenomenon.

EARLY DETECTION ESSENTIAL

Only one of the associations we noted between abnormal bacterial colonisation and poor outcome of pregnancy has been found by others. Kurki *et al*[13] and D A Eschenbach (personal communication) found a similar association between bacterial vaginosis and preterm labour but not between bacterial vaginosis and late miscarriage. The reason for this is not clear. Eschenbach recruited women at a much later stage in gestation than we did, which may account for the failure to associate bacterial vaginosis with late miscarriage, but this explanation is not tenable in the case of Kurki *et al*.[13] Further investigation is required to determine whether the organisms in the intermediate stage are other than those occurring in the flora of grade III. An abnormal outcome of pregnancy in our study was associated also with previous preterm delivery. We emphasise, however, that the effect of the abnormal vaginal flora was an independent predictor of preterm delivery and late miscarriage. Bacterial vaginosis is often a chronic recurrent condition. If it is associated with preterm delivery a weaker association between previous preterm delivery and abnormal flora would be expected.

Our study lacked the power to detect such an association as only 25 women had experienced a previous preterm delivery. A prospective study is required to examine this relation. Whether a combination of the variables mentioned—for example, an abnormal flora together with a history of termination or abortion in an Afro-Caribbean woman—would lead to an even greater chance of an abnormal outcome seems inherently likely but currently the statistical model does not allow us to study this issue.

HOW TO PROLONG GESTATION

The possibility of being able to predict an abnormal outcome in pregnancy so that prophylactic intervention can be instituted is obviously attractive. Lockwood *et al* reported that the detection of fetal fibronectin in cervical and vaginal secretions was predictive of preterm delivery.[15] Thus 49 women with clinical signs of preterm labour whose mean gestational age at sampling was 29·9 weeks delivered when the mean gestational age was 31·3 weeks. Such short warning late in gestation, however, would seem to be of little if any value in effecting an intervention policy to prolong gestation. Indeed, when a group of women at risk of preterm delivery on the basis of detection of fetal fibronectin has been identified the outlook for prevention seems bleak because bed rest, tocolytic treatment, or cervical cerclage[2] have not proved effective in preventing preterm labour. Also, β agonists have come under scrutiny recently,[16] with recommendations for reappraisal of their use because of doubts about safety and efficacy.[17] Admittedly, treatment with erythromycin, despite its relatively narrow range of antibacterial activity, has been reported to delay delivery in a subgroup of women presenting in established preterm labour with cervical dilatation of 1 cm or more.[18] It may be that screening women for infection if they have positive results after fetal fibronectin tests and then treating those in whom infection is found will provide a means of delaying delivery. Detection of risk early in gestation, however, should potentially provide sufficient time to prevent the pathological process rather than reverse it.

Minkoff *et al* recruited women at a mean gestational age of 13·8 weeks and carried out a detailed microbiological analysis.[7] This is expensive and time consuming and may be of use only if conventional sexually transmitted micro-organisms are widely prevalent. Though we do not doubt the value of examining the longitudinal changes in the flora during pregnancy and determining how these correlate with the diagnosis by Gram's method as a means of understanding the pathological events, detailed microbiology is unnecessary in making the diagnosis of bacterial vaginosis. Use of Gram's method should have a much wider practical appeal. In this way it is possible to detect bacterial vaginosis early in pregnancy, either alone or in combination with other variables, and so identify a subgroup of women at increased risk of preterm labour. As a result, it may be possible to reduce the incidence of preterm delivery and late miscarriage by restoring the flora of the lower genital tract to a more benign type dominated by lactobacilli.

Clearly, the approach of intervening with antibiotics requires rigorous assessment with drugs that have activity against the micro-organisms dominating in bacterial vaginosis, such as clindamycin[19] rather than erythromycin.[18 20] Furthermore, it would seem that these might be more effective if, rather than administering them late in pregnancy as they have been up to now,[18 20] they are given early—that is, more on a prophylactic than a therapeutic basis. This would mean treating 15% of pregnant women with an antibiotic.

Clinical implications

- Idiopathic preterm delivery is the most important cause of perinatal mortality and morbidity
- No effective means exist to predict and prevent idiopathic preterm delivery
- This study found that about 15% of pregnant women have abnormal vaginal flora in the form of bacterial vaginosis in early pregnancy
- Women with bacterial vaginosis have fivefold increased risk of late miscarriage or preterm delivery
- Intervention studies are required to determine whether intervention can prevent a woman with bacterial vaginosis having a late miscarriage and preterm delivery

HUMAN AND FISCAL COSTS

In the United States in 1980 it was estimated that the cost of neonatal intensive care exceeded $460m. If all babies had been born healthy at term, it was estimated that this cost would have fallen to $50m. The social and emotional cost of perinatal mortality and morbidity associated with preterm birth is immeasurable. If this treatment is successful it could lead to an overall reduction in the rate of late miscarriage and preterm birth of 30-40% with the associated reduction in the social, emotional, and economical costs. Treatment should be instituted no later than 16 weeks, if possible, to allow prevention of late miscarriage as well as preterm delivery. We are now undertaking a randomised double blind, placebo controlled antibiotic trial along such lines.

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1 Newcombe R, Chalmers I. Assessing the risk of pre-term labour. In: Elder MG, Hendricks CH, eds. *Preterm labour.* London: Butterworths, 1981: 47-60.
2 Hemminki E, Starfield B. Prevention and treatment of premature labour by drugs: review of controlled clinical trials. *Br J Obstet Gynaecol* 1978;85: 411-7.
3 McGregor JA, French JI, Lawellin D, Todd JK. Preterm birth and infection: pathogenic possibilities. *American Journal of Reproductive Immunology and Microbiology* 1988;16:123-32.
4 Romero R, Major M, Wu YK, Sirtori M, Oyarzun E, Mitchell MD, *et al.* Infection in the pathogenesis of preterm labour. *Seminars in Pathology* 1988;12:262-79.
5 Gibbs RS, Romero R, Hillier SL, Eschenbach DA, Sweet RL. A review of premature birth and subclinical infection. *Am J Obstet Gynecol* 1992;166: 1515-28.
6 Lamont RF, Fisk NM. The role of infection in the pathogenesis of preterm labour. In: Studd JWW, ed. *Progress in obstetrics and gynaecology.* Vol 10. Edinburgh: Churchill Livingstone, 1993:135-58.
7 Minkoff H, Grunebaum AN, Schwarz RH, Feldman J, Cummings M, Crombleholme W, *et al.* Risk factors for prematurity and premature rupture of the membranes: a prospective study of the vaginal flora in pregnancy. *Am J Obstet Gynecol* 1984;150:965-72.
8 Gravett MG, Nelson HP, DeRouen R, Critchlow C, Eschenbach DA, Holmes KK. Independent association of bacterial vaginosis and Chlamydia trachomatis infection with adverse pregnancy outcome. *JAMA* 1986;256: 1899-903.
9 Spiegal CA, Amsel R, Holmes KK. Diagnosis of bacterial vaginosis by direct Gram stain of vaginal fluid. *J Clin Microbiol* 1983;18:170-7.
10 Hosmer DW, Lemeshow S. *Applied logistic regression.* New York: Wiley, 1989:80-91.
11 Miettinen OS. Stratification by a multivariate confounder score. *Am J Epidemiol* 1976;104:609-20.
12 Hay PE, Taylor-Robinson D, Lamont RF. The diagnosis of bacterial vaginosis in a gynaecology clinic. *Br J Obstet Gynaecol* 1992;99:63-6.
13 Kurki T, Sivonen A, Renkonen OV, Savia E, Ylikorkala O. Bacterial vaginosis in early pregnancy and pregnancy outcome. *Obstet Gynecol* 1992;80:173-7.
14 Hillier SL, Krohn MA, Nugent RP, Gibbs RS. Characteristics of three vaginal flora patterns assessed by Gram stain among pregnant women. *Am J Obstet Gynecol* 1992;166:938-44.
15 Lockwood CJ, Senyei AE, Dische MR, Casal D, Shah KD, Thung SN, *et al.* Fetal fibronectin in cervical and vaginal secretions as a predictor of preterm delivery. *N Engl J Med* 1991;325:669-74.
16 Canadian Preterm Labor Investigators Group. Treatment of preterm labor with the Beta-adrenergic agonist ritodrine. *N Engl J Med* 1992;327:308-12.
17 Leveno KJ, Cunningham FG. β-adrenergic agonists for preterm labor. *N Engl J Med* 1992;327:349-51.
18 McGregor JA, French JI, Reller LB, Todd JK, Makowski EL. Adjunctive erythromycin treatment for idiopathic preterm labor: results of a randomized, double-blinded, placebo-controlled trial. *Am J Obstet Gynecol* 1986;154:98-103.
19 McGregor JA, French JI, Seo K. Adjunctive clindamycin therapy for preterm labor: results of a double-blind, placebo-controlled trial. *Am J Obstet Gynecol* 1991;165:867-75.
20 McGregor JA, French JI, Richter R, Vuchetich M, Bachus V, Seo K, *et al.* Cervicovaginal microflora and pregnancy outcome: results of a double-blind, placebo-controlled trial of erythromycin treatment. *Am J Obstet Gynecol* 1990;163:1580-91.

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Blood pressure in prospective population based cohort of newborn and infant twins

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Abstract

***Objective*—To describe blood pressure in twins during infancy.**

***Design*—Prospective study of cohort of twins.**

***Setting*—Teaching hospital in Florida.**

***Subjects*—166 viable twin pairs born between July 1976 and December 1989.**

***Main outcome measures*—Blood pressure and body weight at birth, at 14 days, and at 1, 3, 6, 9, and 12 months.**

***Results*—Both systolic and diastolic pressure correlated with body weight throughout infancy (at birth $r = 0{\cdot}41$, $P < 0{\cdot}001$ and $r = 0{\cdot}42$, $P < 0{\cdot}001$ respectively; at 1 year $r = 0{\cdot}23$, $P < 0{\cdot}001$ and $r = 0{\cdot}26$, $P < 0{\cdot}001$ respectively). In infants weighing < 1500 g at birth mean blood pressure rose from about 45/25 mm Hg to 101/55 mm Hg from birth to the age of 1 year, while in infants weighing > 3000 g at birth it rose from 63/39 mm Hg to 100/61 mm Hg; corresponding mean body weights at 1 year were 7·86 kg and 9·88 kg. Differences in birth weight within pairs of monozygotic twins were negatively correlated with such differences in systolic blood pressure at 1 year ($r = -0{\cdot}37$, $P < 0{\cdot}01$).**

***Conclusions*—Blood pressure and body weights in twins showed strongly positive but generally declining correlations throughout infancy. Twins of lower birth weight showed a more rapid rate of rise in blood pressure during infancy. At 1 year the catch up in blood pressure exceeded that in body weight. Greater differences in birth weights between monozygotic twins were associated with smaller differences in systolic blood pressure at 1 year, suggesting that intrauterine environmental factors related to birth weight are important in determining blood pressure in infancy.**

Introduction

Technological advances over the past 20 or so years have improved the accuracy of non-invasive measurements of infant blood pressure. Many investigations have used these techniques to describe blood pressure among infants.[1-12] Data on newborn and infant twins,